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A REVIEW ON SOLID LIPID NANOPARTICLE (SLN): AN ADVANCED TREATMENT MODALITY

Pritee S. Mahajan*, Kishor B Mahajan and A. B. Darekar

R.G. Sapkal College of Pharmacy, Sapkal Knowledge Hub, Kalyani Hills Anjneri Trimbakeshwar, Nashik 422 213 Tal: Tryambakeshwar, Dist: Nashik, Maharashtra, India

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Correspondence to Author:

Pritee S. Mahajan


Master of pharmacy (2nd semester), R.G. Sapkal College Of Pharmacy, Sapkal Knowledge Hub, Kalyani Hills Anjneri Trimbakeshwar, Nashik 422 213 Tal: Tryambakeshwar, Dist: Nashik, Maharashtra, India.

E-mail: Pritimahajan525@gmail.com

ABSTRACT: SLN is a challenging field of nanotechnology notified in the recent years. It has been proved that SLN is more beneficial colloidal drug delivery system because of its more controlled and targeted properties. Recent advances in nanotechnology has indicated unimaginable guarantee to adjust disease therapeutics by creating new treatment modalities which may permit better focused delivery of anticancer medications to destroy dangerous cells in different malignancies. Due to their unique size dependent properties, lipid nanoparticles offer possibility to develop new therapeutics. Parts of SLN stability and the influence of different excipients (utilized as a part of SLN creation) on stability with other optional steps included in their adjustment like freeze drying, spray drying and so on. Issues connected with SLN creation and instrumental strategies utilized as a part of generation are altogether talked about. This review discusses on many aspects of SLN such as its structure, aim, advantages disadvantages, method of sterilization, method of preparation, principle of drug release, route of administration and Its medicinal applications. Study of SLN explores the new ideas in the field of modern pharmaceuticals.

INTRODUCTION: Solid lipid nanoparticles (SLN) presented in 1991 speak to an optional carrier system to convention colloidal carrier, for example, - emulsions, liposomes and polymeric micro – and nanoparticles¹. Nanoparticles produced using solid lipids are drawing in significant consideration as novel colloidal medication carrier for intravenous applications as they have been proposed as an option particulate carrier framework SLN are sub-micron colloidal bearers going from 50 to 1000 nm, which are made out of physiological lipid, scattered in water or in watery surfactant arrangement².

SLN offer special properties, for example, little size, vast surface region, high medication stacking and the communication of stages at the interface and are alluring for their potential to enhance execution of pharmaceuticals Solid lipid nanoparticles are one of the novel potential colloidal transporter frameworks as option materials to polymers which is indistinguishable to oil in water emulsion for parenteral substances. They have numerous focal points, for example, great biocompatibility, low harmfulness and lipophilic medications are better conveyed by robust lipid nanoparticles and the framework is physically steady³.

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Solid lipid nanoparticles (SLNs) are thought to be the best lipid based colloidal bearers, presented in ahead of schedule nineties. This is a standout amongst the most famous methodologies to enhance the oral bioavailability of the ineffectively water solvent medications⁴. SLNs are in the

submicron size scope of 50-1000 nm and are made out of physiologically endured lipid segments which are in solid state at room temperature.⁵

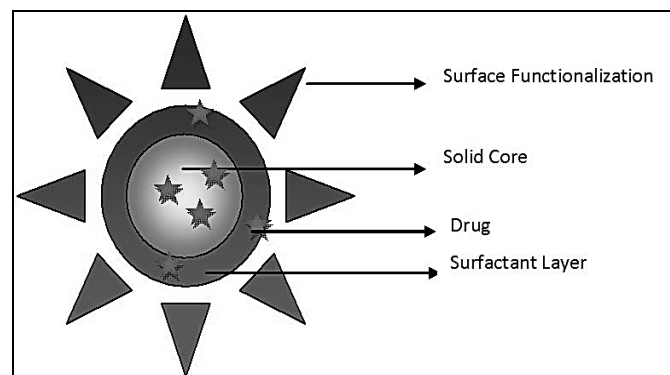


FIG.1: STRUCTURE OF SILID LIPIOD NANOPARTICLES

Aims of solid lipid nanoparticles:

- Possibility of controlled medication release.
- Increased medication solidness.
- High medication pay load.
- No bio-poisonous quality of the bearer.
- Avoidance of natural solvents.
- Inclusion of lipophilic and hydrophilic drugs⁵

Advantages of SLN:

- Control and/ or target medication discharge.
- Excellent biocompatibility.
- Improve stability of pharmaceuticals.
- High and upgraded medication.
- Better control over discharge energy of exemplified mixes.
- Enhanced bioavailability of entangled bioactive mixes.
- Chemical assurance of labile fused mixes.
- Much less demanding to make than biopolymeric nanoparticles.
- No exceptional dissolvable needed.
- Traditional emulsion producing techniques relevant.
- Crude materials fundamental the same as in emulsions.
- High long haul steadiness.
- Application flexibility.⁶

Disadvantages of SLN:

- Molecule development.
- Eccentric gelation propensity.
- Unforeseen motion of polymeric transition⁷.

TABLE 1: LIPIDS AND SURFACTANTS USED IN SOLID LIPID NANOPARTICLES PRODUCTION^{8, 9, 10, 11}

Lipids	Surfactants
Acyl glycerols :	Phospholipids:-
Glycerol monostearate	Soy lecithin
Glycerol behenate	Egg lecithin
Glycerol palmitostearate	Phosphatidylcoline
Triacylglycerol :tricaprin	Ethylene oxide / propylene oxide copolymers:-
Trimyristin	Poloxamer 182
Tristerin	Poloxamer 188
Tripalmitin	Poloxamer 407
Waxes :	Poloxamine 908
Cyclic complexes	Alkylaryl polyether alcohol polymers:-
Cetyl palmitate	Tyloxapol
Cyclodextrin	Bile salt:-
Para-acyl-calix-arenes	Sodium cholate
Fatty acids:	Sodium glycocholate
Stearic acid	Sodium taurocholate
Palmitic acid	Sodium taurodeoxycholate
Behenic acid	Alcohols:-
Decanoic acid	Ethanol, butanol

Sterilization of SLNs:

1. Intravenous and visual organization SLN must be sterile.
2. The high temperature scope amid disinfection via autoclaving causes a hot o/w micro emulsion to structure in the autoclave, alters the extent of the hot nanodroplets.
3. On ensuing moderate cooling, the SLN improved, however some nano-droplets may blend, delivering bigger SLN than the introductory ones.
4. SLN are washed before sanitization, measures of surfactants and co surfactants exhibit the hot frameworks are littler, so that the nano-droplets might be not sufficiently settled¹³.

Principle of Drug Release from SLN:

- ❖ The general standards of medication discharge from lipid nanoparticles are as per the following:

1. There is a converse relationship between medication discharge and the parcel coefficient of the medication.
2. Higher surface territory because of littler molecule measure in nanometer extent gives higher medication discharge.
3. Slow medication discharge can be accomplished when the medication is homogenously scattered in the lipid framework. It depends on sort and medication entanglement model of SLN.
4. Crystallization conduct of the lipid carrier and high portability of the medication lead to quick medication discharge. There is a backwards relationship between crystallization degree and portability of medication. The medication fuse model of SLN is vital to the medication discharge design.
5. Fast initial drug release in the first 5 min in the drug –enriched shell model as a result of the outer layer of particle due to larger surface area of drug depositon on the particle surface.
6. The burst release is reduced with increasing particle size and prolonged release could be obtained when the particles were sufficiently large, i.e., lipid macromolecules.
7. The type of surfactant and its concentration, which will interact with the outer shell and affect its structure, should be noted as the outer factor which is important, because a low surfactant concentration leads to a minimal burst and prolonged drug release.
8. The particle size affect drug release rate directly depends on various parameters such as composition of SLN formulation (such as surfactant, structural properties of lipid, drug)production method and conditions (such as production time, equipment, sterilization and lyophilization)¹⁴

There are 3 drug incorporation model which describe drug release from SLN”

- A) Homogenous matrix model
- B) Drug enriched shell with lipid core
- C) Drug enriched core with lipid shell¹⁵

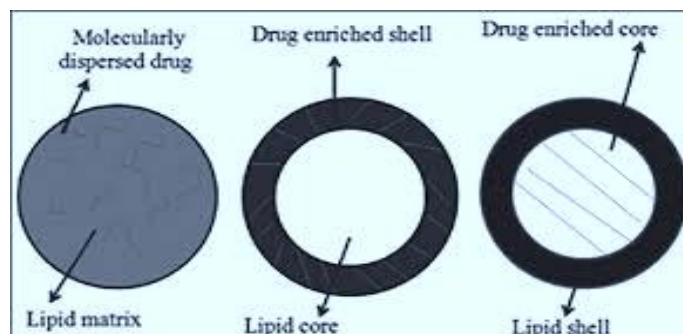


FIG.2: DRUG INCORPORATION MODEL

A) Homogeneous matrix:

Drug being molecularly dispersed is mainly obtained when incorporating highly lipophilic drug into SLN by using hot/ cold homogenization method in cold homogenization technique the drug is dispersed in bulk of melted lipid , then the mechanical force of high pressure homogenization leads to break down of molecular form to nanoparticles and giving rise to homogeneous mixture model.eg. Etomidate SLN represents the homogenous matrix model¹⁵.

B) Drug enriched shell with lipid core model:

Will be obtained when performing production. The drug partitioned to water phase during the production. Cooling, obtained lipid precipitate, due to phase separation it forming practically drug free lipid core. In the meantime, the medication re-segments into the staying aqueous lipid stage and medication fixation in the external shell expanding bit by bit. At long last medication advanced shell solidifies as delineated in **Fig. 2**. The measure of medication parceling to the watery stage will increments with the increment of solvency of medication in the aqueous stage e.g. tetracaine SLN¹⁵.

C) Lipid shell with drug enriched core:

This type of model obtained when dissolving drug e. g. Prednisolone in the lipid melts. In this model, cooling of the shaped nanoemulsion will prompt super saturation of medication in softened lipid and it further leads drug precipitation preceding lipid precipitation. Further cooling will prompt

precipitation of lipid encompassing the medication enhanced center as a layer as showed in **Fig. 2**. Because of expanded diffusional separation and ruining impact of encompassing robust lipid shell, the carrier framework shows managed discharge profile¹⁵.

Various Methods of Preparation of Solid Lipid Nanoparticles:

1. High pressure homogenization

- A. Hot homogenization
- B. Cold homogenization

2. Ultrasonication/high speed homogenization

- A. Probe ultrasonication
- B. Bath ultrasonication

3. Supercritical fluid method
4. Solvent evaporation method
5. Solvent emulsification-diffusion method
6. Microemulsion based method
7. Spray drying method
8. Double emulsion method
9. Precipitation technique
10. Film-ultrasound dispersion
11. Solvent Injection Technique.
12. Using membrane contractor.

A) High Pressure Homogenization (HPH):

1. It is a reliable and powerful technique, which is used for production of SLNs.¹⁶
2. High pressure homogenization push a liquid with high pressure(100-2000 bar) through a narrow gap.¹⁷
3. The fluid accelerate on a very short distance to very high velocity(over 100 km / hr)
4. Very high shear stress and cavitation forces disrupt the particles down to the submicron range.¹⁸
5. Generally 5-10% lipid content is used but up to 40% lipid content has also been investigated.¹⁹

a) Hot Homogenization:

1. Hot homogenization is carried out at temperature above the melting point of the

lipid and can therefore be regarded as the homogenization of an emulsion.²⁰

2. A pre-emulsion of the drug loaded lipid melt and the aqueous emulsifier phase is obtained by high shear mixing device.²¹
3. HPH of the pre-emulsion is carried out at temperature above the melting point of the lipid.²²
4. In general higher temperature in lower particle size due to the decreased viscosity of the inner phase.²³
5. However, high temperatures increase the degradation rate of the drug and the carrier.
6. Increasing the homogenization pressure often result in an increase of the particle size due to high.
7. Kinetic energy of the particles.

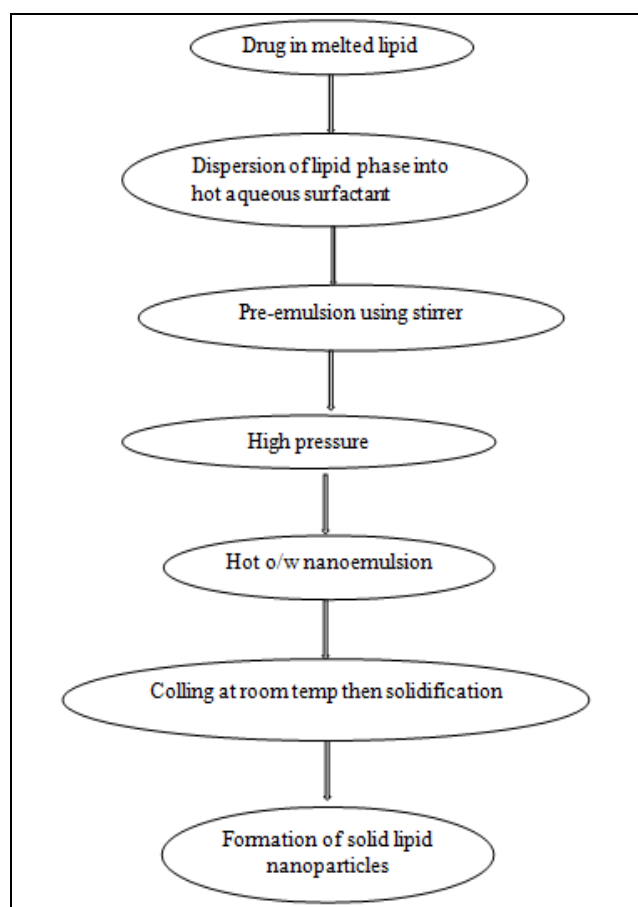


FIG.3: SOLID LIPID NANOPARTICLES BY HOT HOMOGENIZATION

b) Cold homogenization:

1. Cold homogenization has been developed to overcome various problem associated with hot homogenization.²⁰

- Drug degradation due to temperature.

- Drug distribution in the aqueous phase at the time of homogenization.

- Complexity of the crystallization step of the nanoemulsion leading to several modification and/or super cooled melts.

1. In this drug technique the drug containing lipid melt is brought to the lower temperature, the solid lipid ground to lipid micro particles and these lipid micro particles are dispersed in a cold surfactant solution yielding a pre-suspension.²¹
2. Then this pre-suspension is homogenized at or below room temperature, the gravitation force is strong enough to break the lipid microparticles directly to solid lipid nanoparticles.²²

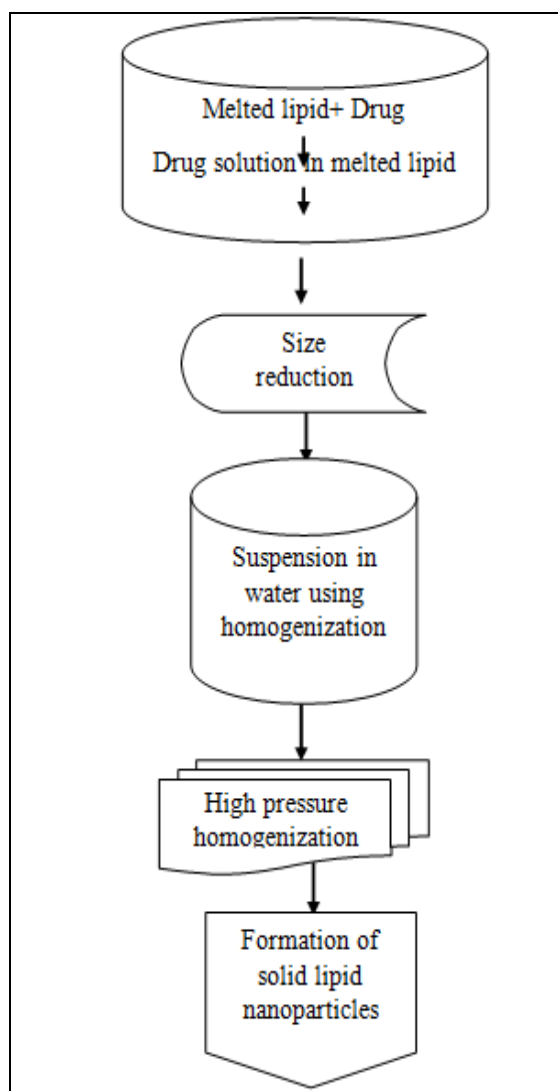


FIG.4: SOLID LIPID NANOPARTICLES BY COLD HOMOGENIZATION

Advantages:

- Demonstration at lab scale.
- Low capital cost²³

Disadvantages:

- Polydisperse distribution.
- Experimentation at lab scale biomolecule damage.
- Energy intensive process.
- Unproven scalability²³

B) Ultrasonication / high speed homogenization:

SLNs are also prepared by this technique. For smaller particle size combination of both ultrasonication and high speed homogenization is required.²⁴

Advantage:

- Reduced shear stress.²³

Disadvantages:

- Structural instability such as particle growth upon storage.
- Potential metal contamination²³

C) Solvent emulsification- diffusion method:

1. The particle with average diameter of 30-100 nm can be obtained by this technique.²⁵
2. Avoidance of heat during the preparation is the most important advantage of this technique.
3. In this technique lipid are generally dissolved in the organic phase in water bath at 50°C and used an acidic aqueous phase in order to adjust the zeta potential to form conservation of SLN, and then easy separation by centrifugation.²⁶
4. The SLN suspension was quickly produced.
5. The entire re-dispersed system can then be centrifuged and re-suspended in distilled water.²⁷

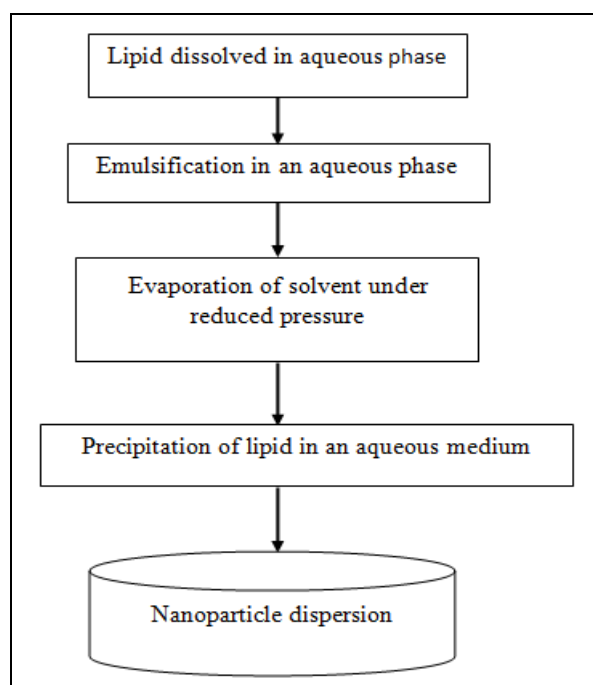


FIG.5: SOLVENT EMULSIFICATION DIFFUSION METHOD

D) Supercritical fluid method:

1. This is relatively new technique for SLN production and has the advantage of solvent-less processing.
2. There are several variation in this platform technology for powder and nanoparticle preparation.
3. SLN can be prepared by the rapid expansion of supercritical carbon dioxide solution method.²³

Advantages:

- Avoid the use of various solvents.
- Environmental conditions of Temperature and mild pressure.
- Instead of suspensions particles are obtained as a dry powder.
- Carbon dioxide solution is the best solvent for this method.²³

E) Microemulsion based method:

1. This method is based on the dilution of microemulsions.
2. As micro-emulsions are two-phase system composed of an inner and outer phase(eg. o/w microemulsion)
3. They are made by stirring an optically transparent mixture at 65-70°C, which

typically composed of a low melting fatty acid (e.g. Stearic acid), an emulsifier (e.g. polysorbate 20), co-emulsifier (e.g. butanol) and water²⁴

4. The hot microemulsion is dispersed in cold water (2-3°C) under stirring.
5. SLN dispersion can be used as granulation fluid for transferring in to solid product by granulating process, but in case of low particle content too much of water need to be removed²⁸
6. High temperature gradients facilitate rapid lipid crystallization and prevent aggregation.²⁹

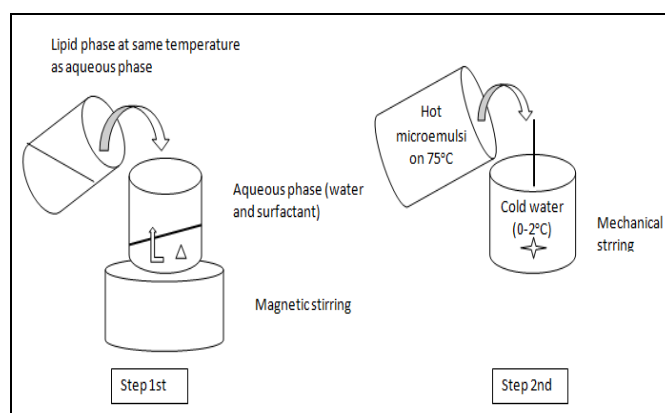


FIG. 6: EMULSIFICATION BASED METHOD

Advantages:

- Low mechanical energy input.
- Theoretical stability.²³

Disadvantages:

- Labor intensive formulation work.
- Extremely sensitive to change.
- Low nanoparticle concentration.²³

F) Spray drying method:

1. This is an alternative technique to the lyophilization process.
2. This recommends the use of lipid with melting point more than 70°C
3. The best results were obtained with SLN concentration of 1% in a solution of terhalose in water or 20% terhalose in ethanol-water mixture.³⁰

G) Double emulsion method:

1. Here the drug is encapsulated with a stabilizer to prevent the partitioning of drug

into external water phase during solvent evaporation in the external water phase of w/o/w double emulsion.

2. Warm w/o/w double micro emulsion can be prepared in two steps.
3. Firstly, w/o microemulsion is prepared by adding an aqueous solution containing drug to mixture of melted lipid, surfactant and co-surfactant to obtain a clear system.
4. In second step, formed w/o microemulsion is added to a mixture of water, surfactant, co-surfactant to obtain a clear w/o/w system.
5. SLNs can be obtained by dispersing the warm micro double emulsion in cold then washed with dispersion medium by ultra filtration system.³¹

H) Precipitation method:

1. The glycerides are dissolved in an organic solvent (e.g. Chloroform) and the solution will be emulsified in an aqueous phase.
2. After evaporation of the organic solvent the lipid will be precipitated forming nanoparticles.²³

I) Film ultrasound dispersion:

1. The lipid and the drug were put into suitable organic solutions, after decompression, rotation and evaporation of that solution, a lipid film is formed. Then the aqueous solution which includes the emulsion was added.
2. Using the ultrasound with the probe to diffuser at the end, the SLN with the little and uniform size particles are formed.²³

J) Membrane contractor method:

1. The present study investigates a new process for the preparation of SLN using a membrane contractor, to allow large scale production.
2. The lipid phase is pressed, at a temperature above the melting point of the lipid, then the small droplets are formed by allowing the liquid to pass through the membrane pores.
3. The aqueous phase circulates inside the membrane module, and then the droplets form at the pore outlets are swiped away.

4. SLN are formed by the following cooling of the preparation to room temperature.
5. The influence of process parameters (aqueous phase and lipid phase temperature, aqueous phase cross-flow velocity and lipid phase pressure, membrane pore size) on the SLN size and on the lipid phase flux is investigated.
6. Also, vitamin E loaded SLN are prepared, and their stability is demonstrated.³²

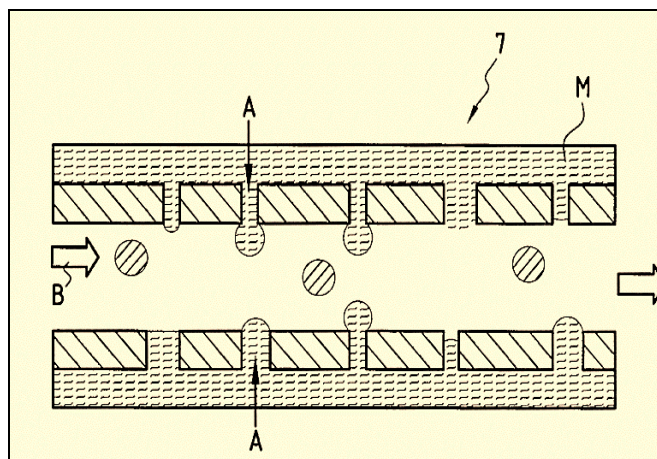


FIG. 5: MEMBRANE CONTRACTOR

Where,

A- Lipidphase,

B- Water phase,

M-Porous membrane,

7-TangentIdeal flow filtration unit.

Secondary production steps:²³

- ✓ Freeze drying
- ✓ Sterilization
- ✓ Spray drying

Problems associated with SLN preparation:

- ❖ High pressure induced drug degradation
- ❖ Lipid crystallization and drug incorporation
- ❖ Lipid modification
- ❖ Particle shape
- ❖ gelation phenomenon
- ❖ super cooled melt³³

Route of administration and biodistribution of SLN:

The *in vivo* behavior of the SLN particle will mainly depend on the following point: Interaction of the SLN with the biological surrounding including: distribution processes and enzymatic processes.

Various routes of administration are as below:

TABLE 2: TECHNIQUES AND WHICH SOLVENTS USED IN THAT PREPARATION METHOD

Technique	Particle size	Solvent used	Instrumentation needed	Working temperature	Operating conditions
High pressure homogenisation	50-1000 nm		High pressure homogeniser	5-10°C upon lipid mp	cavitation forces
High shear homogenisation	50-1000 nm		High shear homogeniser	5-10°C upon lipid mp	Ultrasound treatment
Ultrasound homogenisation	50-1000 nm		Ultrasound apparatus	5-10°C upon lipid mp	
Melt dispersion	1-250 µm		High shear homogeniser	5-10°C upon lipid mp	
PIT	30-100 nm			90°C	
Microemulsion dilution	50-800 nm			5-10°C upon lipid mp	pH shifts
Microemulsion cooling	50-300 nm			37-55°C	
Coacervation	200-1000 nm			40-75°C, according to the lipid matrix	
Solvent injection	100-500 nm	Ethanol, acetone, isopropanol		25°C	
Solvent evaporation from emulsions	30-500 nm	Chlorinated solvents	High shear/pressure homogeniser	25°C	
Solvent diffusion from emulsions	100-2000 nm	Partially water miscible solvents	High shear/pressure homogeniser	40-50°C	
PGSS	0.2-20 µm		GAMA apparatus	5-10°C upon lipid mp	Pressure>74 bar
SFEE	20-90 nm	Chlorinated solvents	High pressure homogeniser SFEE apparatus	>31°C	Pressure>74 bar
Cryogenic micronisation	1-500 µm			-80°C	
Membrane contactor method	100-200 nm		Membrane contactor	5-10°C upon lipid mp	
Spray-drying	0.3-10 µm	Ethanol	Spray-drier	70°C	
Electrospray	Nearly 1 µm	Aliphatic alcohols	Electrospray apparatus	25°C	High voltage
Spray-congealing	50-2000		Spray-congealing	5-10°C upon	

TABLE 3: SHOWS LIST OF DRUG INCORPORATED IN SLN³⁵

Pharmacological category	Drugs
Anticancer Drugs	Camptothecin Etoposide Paclitaxel, Docetaxel Vinorelbine, Vinpocetine Doxorubicin, Idarubicin, Adriamycin, Mitoxantrone Methotrexate, 5-Fluorouracil Oxaliplatin, Tamoxifen, Ubidecarenone, Cholesteryl Butyrate, Chlorambucil, Temozolomide, β-elements, Podophyllotoxin, All trans retinoic acid ³⁵
Cardiovascular Drugs	Verapamil, Nifedipine, Nitrendipine.
Hormonal Drugs	Hydrocortisone, Cortisone, Prednisolone, Deoxycorticosterone, Progesterone, Estradiol, Mifepristone, Betamethasone, Sildenafil Citrate, Insulin ³⁶ .
Vitamins	Vitamin-A, Vitamin-E, Vitamin-K, Ascorbyl Palmitate, Retinol.
NSAIDS	Ibuprofen, Flurbiprofen, Diclofenac, Nimesulide, Naproxen, Ketorolac ³⁷
Antifungal Drugs	Ketoconazole, Miconazole, Itraconazole, Econazole, Terbinafine, Amphotericin.
Antibacterial Drugs	Ciprofloxacin, Tobramycin, Clotrimazole
Antitubercular Drugs	Rifampicin, Isoniazid, Pyrazinamide.
Antiviral Drugs	Aciclovir, Saquinavir, Penciclovir, Adefovir, Dipivoxil, Thymopentin, 3-Azida-3-deoxyuridine, Oxymetrine, Quinine, Chloroquine ³⁸ .
Drugs acting on Nervous System	Diazepam, Oxazepam, Carbamazepine
Anxiety and Epilepsy	Clozapin, Olanzapin
Antipsychotic Drugs	Piribedil
Parkinson's disease Drugs	
Immunosuppressant Drugs	Cyclosporin, Tacrolimus
Miscellaneous Drugs	Timolol, Pilocarpine, Tetracaine.
Glaucoma Drugs	Lovastatin, Simvastatin
Hypolipidaemic Drugs	Etomidate
Anaesthetic drugs	Actarit
Antiarthritic Drugs	Reserpidone
Adrenergic Drugs	Domperidone
Antiemetic Drugs	Praziquantel
Anthelmintic Drugs	Sodium Cromoglycate
Other Drugs	Diminazine, Gamma Oryzanol, Calixarene, Resveratrol, Taspine, Apolipoprotein P, Tashione.

1. Parenteral administration:

- a) Peptide and proteins drugs are usually available for parenteral use in the market.
- b) Since their conventional oral administration is not possible due to enzymatic degradation in GI tract.
- c) Parenteral application of SLN reduces the possible side effects of drug incorporated with the increased bioavailability. These system are very suitable for drug targeting³⁴

2. Oral Administration:

- a) Controlled release behavior of SLNs is reported to enable the bypass of gastric and intestinal degradation of the encapsulated drug, and their possible uptake and through the intestinal mucosa.
- b) However, the assessment of the stability of colloidal carrier in GI fluids is essential in order to predict their suitability for oral administration.

3. Rectal administration:

- a) When rapid pharmacological effect required, in some circumstances, parenteral or rectal administration is preferred.
- b) This route is used for pediatric patient due to easy application.

4. Nasal administration:

- a) Nasal route preferred due to its fast absorption and rapid onset of drug action also avoiding degradation of labile drugs in the GIT and insufficient transport epithelial cell layer³⁴

5. Respiratory delivery:

- a) Nebulization of solid lipid particle carrying anti-tubercular drugs, anti-asthmatic drug and anti-cancer was observed to be successful in improving drug bioavailability and reducing the dosing frequency for better management of pulmonary action³⁴

6. Ocular administration:

- a) Biocompatibility and muco-adhesive properties of SLN improve their interaction with ocular mucosa and prolong corneal

residence time of the drug with the aim of ocular drug targeting²³

7. Topical administration:

- a) SLN are very attractive colloidal carrier system for skin application due to their various desirable effect on skin besides the characteristics of a colloidal carrier system³⁴
- b) They are well suited for use on damaged or inflamed skin because they are based on non-toxic lipids.

Application of SLN:**A) SLN as potential new adjuvant for vaccines:**

1. Adjuvant are used in vaccination to enhance the immune response
2. The safer new subunit vaccines are less effective in immunization and therefore effective adjuvant are required.
3. New development in the adjuvant area are the emulsion systems.
4. These are oil-in-water emulsions that degrade rapidly in the body.
5. Being in the solid state the lipid components of SLNs will be degraded more slowly providing a longer lasting exposure to the immune system.³⁹

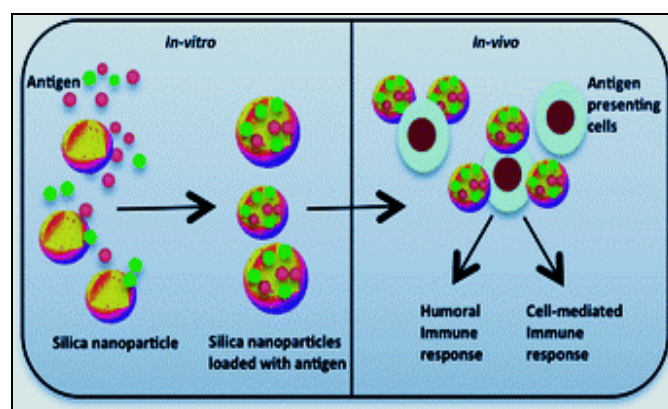


FIG. 6: SLN AS POTENTIAL NEW ADJUVANT FOR VACCINES

B) Solid lipid nanoparticles in cancer chemotherapy:

1. From the last two decades several chemotherapeutic agents have been encapsulated in SLN and their *in-vitro* and *in-vivo* efficacy have been evaluated.

2. Outcome of these studies have been shown to improve the efficacy of chemotherapeutic drugs and also it was found that there are less side effects associated with them.
3. Improved stability of drugs, encapsulation of chemotherapeutic agents of diversified physicochemical properties, enhanced drug efficacy, improved pharmacokinetics and less *in-vitro* toxicity are the important

feature of SLN which make them a suitable carrier for delivering chemotherapeutic drugs.

4. Several obstacles frequently encountered with anticancer compounds, such as normal tissue toxicity, poor specificity and stability and a high incidence of drug resistant tumor cell, are at least partially overcome by delivering them using SLN.⁴⁰

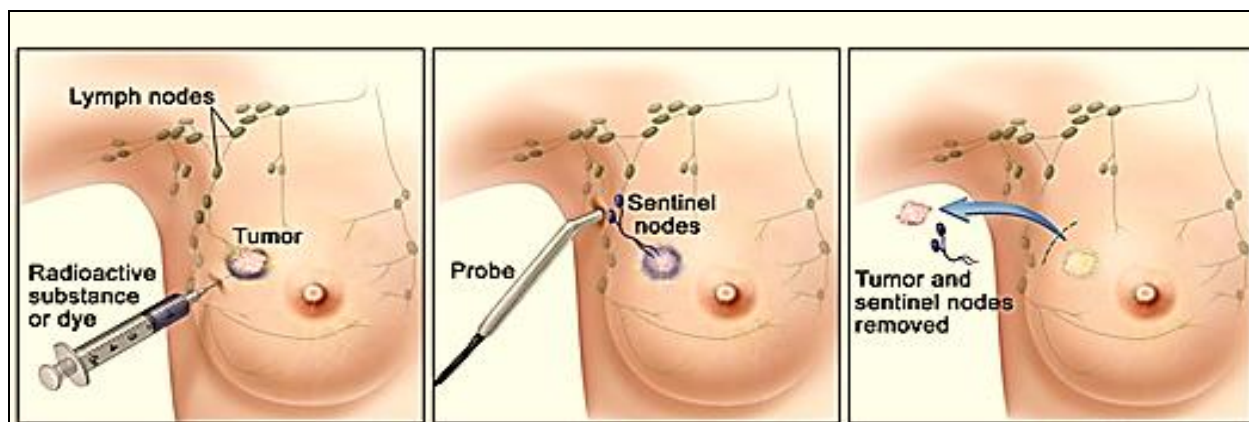


FIG.7: SOLID LIPID NANOPARTICLES IN CANCER CHEMOTHERAPY

a) SLN as targeted carrier for antineoplastic drug to solid tumor:

- ❖ Tamoxifen is an anticancer drug inserted in SLN to prolong the release of drug after IV administration in breast cancer.
- ❖ Tumor is targeted with SLN loaded with drug like methotrexate and camptothecin⁴¹

b) SLN in breast cancer and lymph node metastate:⁴⁰

- ❖ Mitoxantrone SLN administered to reduce the toxicity and improve the safety and bioavailability of the drug⁴¹

C) SLN for targeted brain drug delivery:⁴⁵

1. The extremely small particle size of SLN, which are less than 50 nm, might be beneficial with respect to drug targeting.
2. Drug targeting might also be possible by surface modification of solid lipid nanoparticles.
3. SLNs can improve the ability of the drug to penetrate through the blood brain barrier and is a promising drug targeting system for

the treatment of central nervous system disorders.

4. In a study to overcome the limited access of the drug 5-fluoro-2'-deoxyuridine to the brain, 3',5'-dioctanoyl-5-fluoro-2'-deoxyuridine was synthesized and incorporated into SLN.(DO-FUdR to DO-FUdR-SLN).
5. The potential advantage of the use of solid lipid nanoparticles over polymeric nanoparticles are accounted on the bases of a lower cytotoxicity, higher drug loading capacity and the best production scalability.

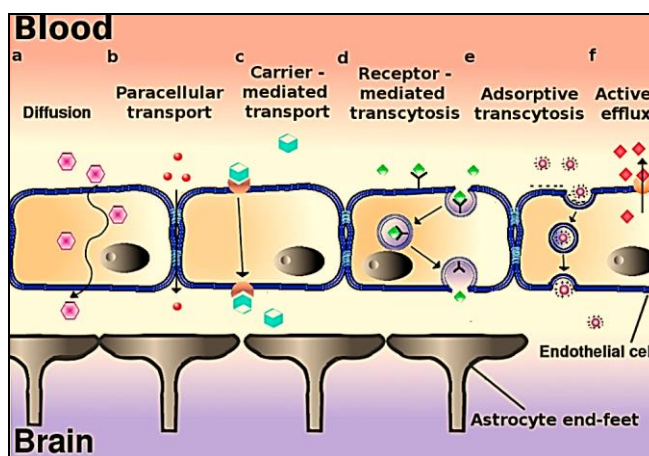


FIG. 8: SLN FOR TARGETED BRAIN DRUG DELIVERY

D) Solid lipid nanoparticles for parasitic disease:

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1. Parasitic disease like (malaria, leishmaniasis, trypanosomiasis) are one of the major problem around the globe.
2. Ant parasitic chemotherapy is the only choice of treatment for these parasitic infections, the reason for this is that these infection do not elicit pronounced immune response hence effective vaccination may not be possible.
3. SLNs and non-structured lipid carriers (NLCs) represent a second generation of colloidal carrier and have emerged as an effective alternative to liposomes mainly

due to their better stability profile, ease of scalability and commercialization and relative cost efficacy.

4. SLN and NLC due to their particulate nature and inherent structure exhibit good potential in the treatment of parasitic infection.
5. However, the need of hour is to undertake extensive investigation on SLN and NLC matrices in order to extend their versatility with respect to encapsulation ability and target ability and to arrive at a versatile, effective and economical approach for the delivery of anti-parasitic drug.

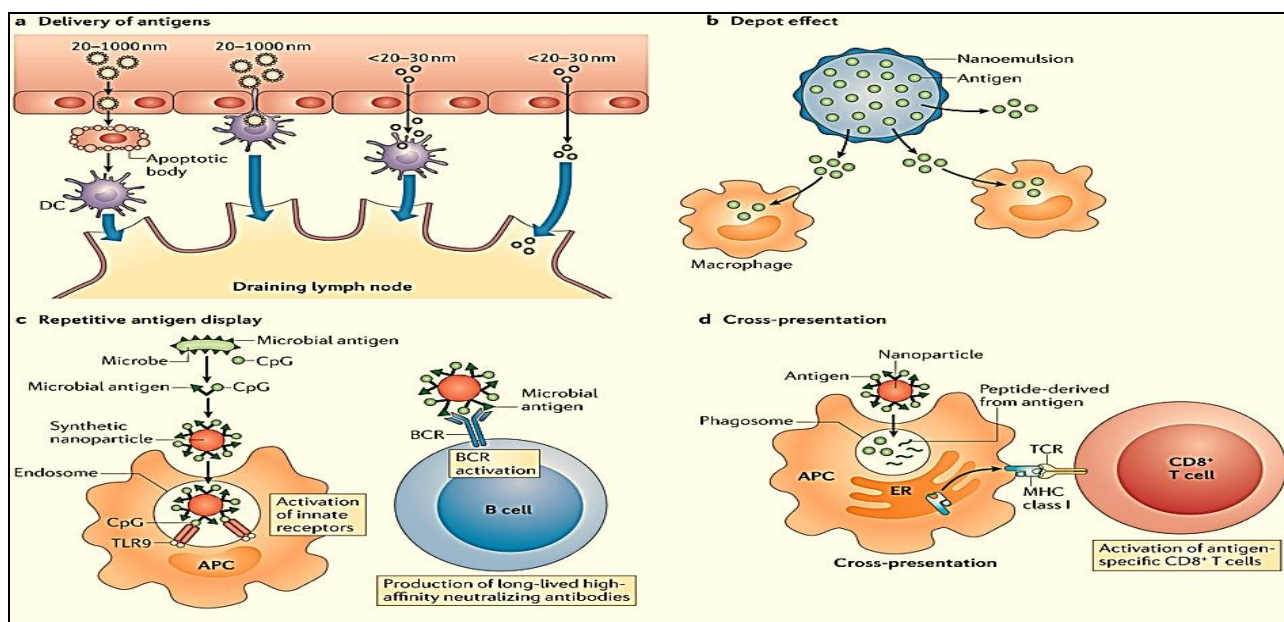


FIG. 9: SOLID LIPID NANOPARTICLES FOR PARASITIC DISEASE

E) SLN in tuberculosis disease: 44

1. SLN have longer stability and better encapsulation efficiency than liposome and as opposed to polymeric nanoparticles, the production process involves minimal amount of organic solvent.
2. SLN have been used to encapsulate Anti Tubercular Drug (ATD) and were proved to be successful in experimental tuberculosis.
3. Antitubercular drugs such as rifampicin, isoniazid, and pyrazinamide SLN system were able to decrease the dosing frequency and to improve patient compliance.

4. ATD were co-incorporated into SLN to evaluate the potential of these carrier in tuberculosis chemotherapy via the oral route.

5. The finding of this study suggested that SLN have great potential in the delivery of ATD by reducing frequency of doses and improving patient compliance by better management of tuberculosis.

F) SLN for lymphatic targeting:

The solid lipid nanoparticles were developed and evaluated for the lymphatic uptake after intraduodenal administration to rats.

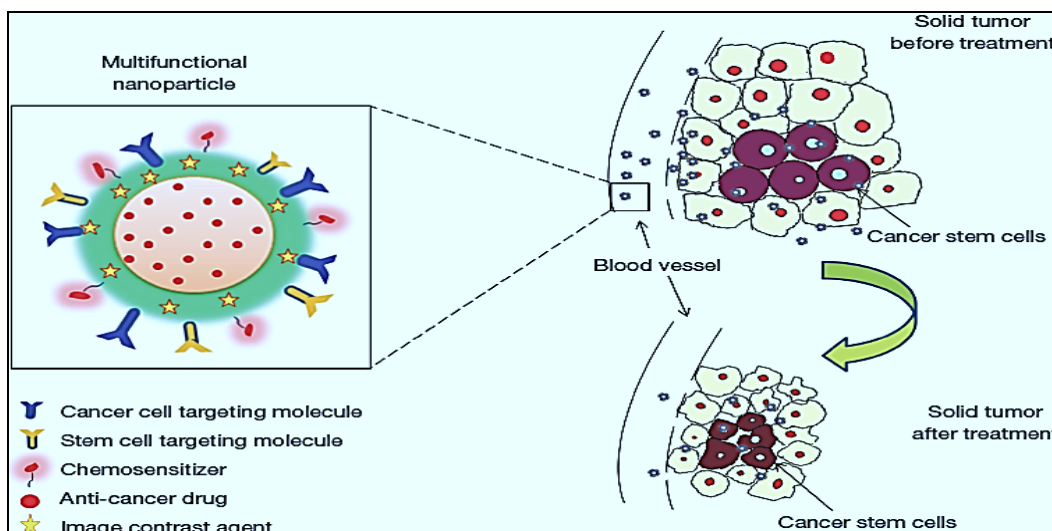


FIG.10: SLN IN TUBERCULOSIS DISEASE

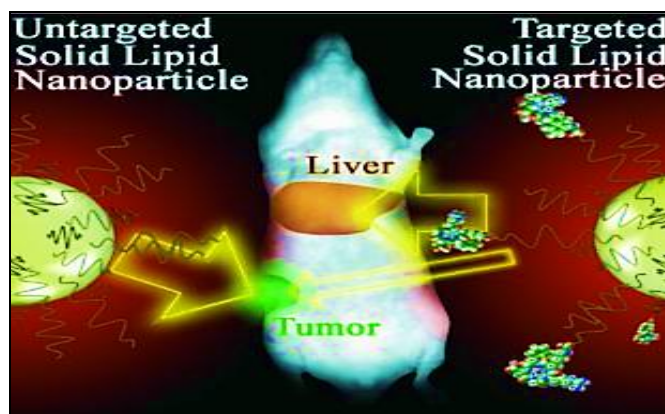


FIG. 11: SLN FOR LYMPHATIC TARGETING

G) Stealth nanoparticles on anti-cancer drug delivery:

1. These give a novel and remarkable medication conveyance framework they dodge fast leeway by the resistant framework.

2. Such nanoparticles can target particular cells. Stealth SLNs have been effectively tried in creature models with marker particles and medications.
3. Immunizer marked stealth Lipobodies have demonstrated expanded conveyance to the target tissue in available destinations.

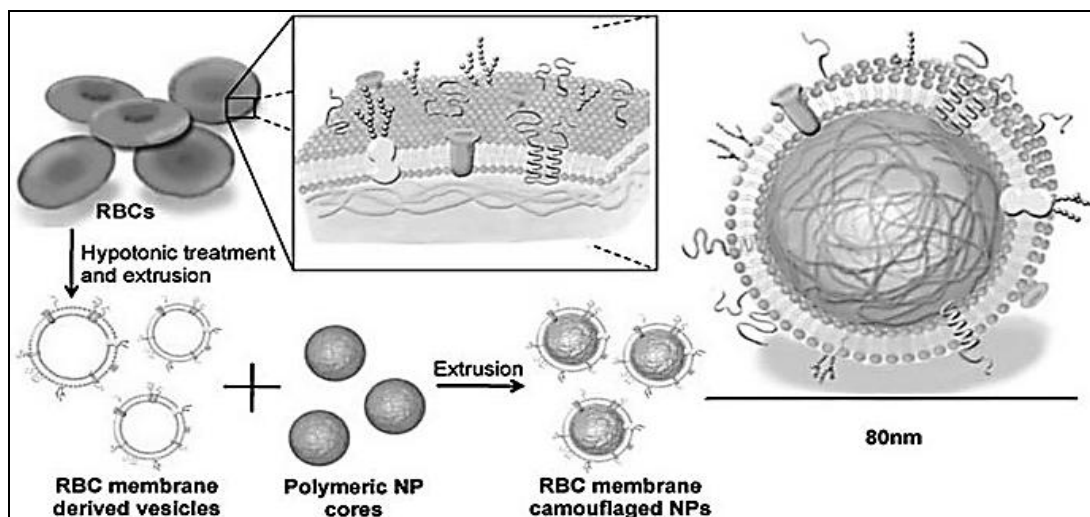


FIG. 12: STEALTH NANOPARTICLES ON ANTI CANCER DRUG DELIVERY

Cosmeceuticals:

The SLNs have been connected in the preparation of sunscreens and as a dynamic transporter operators for molecular sunscreens and UV blockers. SLN and NLCs have turned out to be controlled release innovative occlusive topical. Better localization has been attained to for vitamin in upper layers of skin with glyceryl behenate SLNs analyzed to conventional formulation.

1. SLNs as gene vector carrier:

- SLN can be utilized as a part of the quality vector formulation.
- There are a few late reports of SLN convey hereditary/peptide materials such as DNA, plasmid DNA and other nucleic acids.
- The quality exchange was enhanced by incorporation of a polar HIV-1 HAT peptide (TAT 2) into SLN quality vector.
- The lipid nucleic acid nanoparticles were readied from a liquid nanophase containing water and a water miscible natural dissolvable where both lipid and DNA are independently broken /down by uprooting the organic dissolvable, stable and homogeneously sized lipid-nucleic corrosive nanoparticle (70-100 nm) were formed.
- It's called genospheres. It is targeted specific by insertion of a neutralizer lipopolymer conjugated in the molecule.

2. SLN in breast cancer and lymph node metastate:

- Mitoxantrone-stacked SLN neighborhood infusions were formulated to diminish the poisonous quality and enhance the safety and bioavailability of medication.
- Adequacy of doxorubicin (Dox) has been accounted for to be enhanced by consolidation in SLNs.
- In the methodology the Dox was complexed with soybean-oil-based anionic polymer and dispersed together with a lipid in water to form Dox-stacked solid lipid nanoparticles.
- The system has upgraded its viability and diminished breast cancer cells.

3. SLN as a targeted carrier for anticancer drug to solid tumors:

- Have been accounted for to be valuable as drug carriers to treat neoplasms.
- Tumor targeting has been accomplished with SLNs stacked with medications like methotrexate and Camptothecin.
- Tamoxifen an anticancer medication is joined in SLN to draw out arrival of medication after I.V.

4. SLNs for potential agriculture application:

- Crucial oil extricated from Artemisiaarborescens L when joined in SLN, were able to lessen the fast vanishing compared with emulsions and the frameworks have been used in horticulture as a suitable transporter of naturally protected pesticides.

Evaluation of Solid Lipid Nanoparticles:

The important parameters which need to be evaluated for the SLNs are,

1. Particle size
 - a) Atomic force microscopy
 - b) Photon force microscopy
 - c) Static light Scattering diffraction
 - d) Nuclear magnetic resonance
 - e) Electron Microscopy
 - f) X ray Diffraction
2. Zeta potential
3. Entrapment efficiency
4. Methods for the assessment of drug release from SLN
5. Sterilization of SLN
6. Measurement of crystallinity and lipid
7. Storage stability

CONCLUSION: solid lipids which remains in solid state at room temperature and body temperature, instead of liquid oils is very attractive to achieve controlled drug release, leads to the formation of solid lipid nanoparticles (SLN) at the beginning of the 1990's. The SLN combine advantages of solid particles, emulsions and liposomes. The site specific and sustain release effect of drug can better achieved by using solid lipid nanoparticles (SLN). Nanoparticles have been used extensively for application in drug discovery, drug delivery, diagnostic and for many other in medical field. It is well documented that colloidal drug delivery system could increase drug loading

and could reduce toxicity associated with drug administration. They are relatively novel drug delivery system and further hold great promise for its systemic research. An approach undertaken here is to focus on various production methods introduced till date, and are capable for bulk production.

In addition, a wide medicinal application of SLNs in drug delivery and relevant technology have been discussed. Diverse instrumental techniques have been highlighted to characterize the physiochemical properties of SLNs. Various mode of administration for SLNs are logistically reviewed and discussed.

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